PATENT SPECIFICATION

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COMPLETE SPECIFICATION

Anti-rheumatic Suppository

I, PAULO SEABRA, a Citizen of Brazil residing at Rua Ferreira Pontes 148, Rio de Janeiro, Brazil, do hereby declare the invention, for which I pray that a patent may be granted to me, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to an anti-rheumatic suppository.

The use of cortisone and other hormones in the treatment of rheumatism has been questioned due to the effect of such hormones on active and apparently inactive tuberculosis, occasioning a revival of interest in salicylates as a treatment for rheumatism. As a matter of fact, it has been shown that cortisone and other hormones act in the same manner as salicylates on rheumatic tissue by inactivating hyaluronidase.

However, the conventional salicylate treatment has many disadvantages. For example, tests have shown that the intravenous administration of salicylates has no superiority over the oral administration, resulting in the adoption of the latter with the only modification of coating the tablets with keratin, which coating is not without its unfavourable effects on the patient. Heretofore, it has been held that in the administration of sodium salicylate in rheumatic infections (acute or sub-acute), edema of the affected tissues is an important factor in the production of pain and impairment of motion, and that the therapy indicated is therefore that of inducing dehydration. In the intricate bio-chemistry of edema, rigorous analysis of urine samples has shown a constant retention of sodium that varies directly with the severity of the illness. Patients with hepatic scirrhus have shown great sodium reduction in their urine, some presenting only traces. Other studies have shown that during the acute stage of rheumatism, at the moment of polyarthritis, a decrease in sodium chloride in the urine has been noted. Therefore, the rheumatic patient may be subjected to the discomfort of a lower salt diet which according to certain authorities is effective only if the total nyctohemeral intake is less than one gram of salt. Consider then the error of treating the patient at the same time with six, eight or sixteen grams of another compound, namely, the salicylate, which carries in these doses respectively two, three and six times more sodium, the edema-inducing metal.

Instead of administering sodium salts of the salicylate, it is possible to employ instead the calcium salts, since sodium and calcium are ionic antagonists in all physiological reactions. In fact, it has been demonstrated that the increase of sodium in relation to calcium is occasioned by the afflux of water from the serum to the tissues. The serologic relation of sodium to calcium (it normally being 33) increases in the edematous patient, either due to the excess of sodium or lack of calcium, as may be seen from the following table:

Serologic Relation Sodium to Calcium

Normal Persons	33
Patient: Cardiac Asystolic	54.7
Patient: Cardiac Asystolic	61.0
Patient: Azotemic Nephritis	38.3
Patient: Nephritis	34.6
Patient: Hypertrophic Ethylic Cirrhosis	39.0
Patient: Nephrosis	54.1
Patient: Nephrosis	64.0
Patient: Nephrosis	80.0

The diuretic action exercised by calcium salts is independent of the acid with which it is combined. Calcium, when mobilizing the liquid of articular edemas is very often accompanied with slight pain exacerbation, which usually occurs also with the use of radio therapy, cortisone, and corticotropin. One authority, administering calcium in com-

[Price 3/-]

bination with a weak acid, i.e., calcium gluconate, observed acute exacerbation followed soon by remission, effecting complete cure in twenty-three cases of acute rheumatism and twenty-eight of chronic rheumatism, restoring articular mobility, normalizing the erythrocytic sedimentation, and showing cardiac improvement without relapse during one year of observation. This authority attributes great importance to the desensitizing role also performed by the calcium.

The problem resides in the manner of administration of the drug. Since in attempting to have the salicylic acid reach the arterial blood, the salicylic acid is fixed by the cartilagenous tissue with astonishing selectivity. However, a very small dose of salicylate is sufficient if it reaches the arterial blood, because while such a dose is small when compared with the total weight of the body, it is no longer as small when compared with the weight of the cartilage, which also is small. When administered orally in small doses, the salicylic acid does not reach the arteries because it is detained by the liver. In fact, the salicylate effects a special hepatotoxic action on the liver, which further accentuates the unfavourable effects produced by the rheumatic disease. The first thing the salicylate does when it reaches the liver is to paralyze the glycogenesis in the already damaged liver. Thus, a struggle is drawn between the liver and the salicylate, which latter is administered daily in ever increasing doses up to six, eight and sixteen grams in the hope that a small portion reaches the arteries while the liver is being increasingly damaged.

It is accordingly a principal object of the present invention to provide an anti-rheumatic suppository effective in the treatment of rheumatism wherein the small and effective dose of salicylate required is introduced into the arterial blood without passing through the liver.

It is still another object of the present invention to provide an anti-rheumatic mixture of the above type wherein the active principle is absorbed during rectal administration by the inferior hemorrhoidal plexus, the principle then passing to the median and inferior hemorrhoidal veins and reaching the heart without passing through the liver.

Other objects and the advantages and nature of my improved anti-rheumatic suppository will be apparent from the following description of the ingredients making up the same, the proportions thereof, the method of preparation and the manner in which the aforesaid anti-rheumatic mixture is to be used.

My improved formula for making the anti-rheumatic suppository contains the following thoroughly admixed ingredients: Salicylic acid, calcium carbonate and an inactive base to insure the necessary consistency of a suppository.

I have found that a mixture of salicylic acid, calcium carbonate and polyethylene glycol yields the best results, although mixtures containing other inept bases, such as hypocola (fish glue, gelatin) or cocoa butter may be used in place of polyethylene glycol.

I prefer to make up the above described mixture in the following proportions:

24 parts by weight of salicylic acid 12.5%
8 parts by weight of calcium carbonate
160 parts by weight of polyethylene glycol 83.5%

The above proportions of my mixture may be considerably varied without effecting its efficiency and the above proportions are set forth merely to illustrate a formula that I have found to work well in practice.

The suppository is prepared by thoroughly mixing 24 parts by weight of salicylic acid and 8 parts by weight of calcium carbonate. To the resulting powder, 160 parts of polyethylene glycol are added in a mechanical homogenizer. The resulting mixture is placed in a sterilizer and heated to 120 degrees C. for a half hour, care being taken to permit the escape of any gas that is formed.

Tests have shown that this anti-rheumatic mixture when administered in the form of a suppository spares the liver and introduces the small but effective dose of salicylate in the arterial blood, the active principle being absorbed by the inferior hemorrhoidal plexus, passing through the median and inferior hemorrhoidal veins and finally reaching the heart without passing through the liver. The anti-rheumatic quality of this suppository results from the calcium salicylate formed in the mixture.

What I claim is:—

1. An anti-rheumatic suppository comprising an inert substance suitable for rectal administration having the necessary consistency of a suppository, and calcium salicylate.

2. An anti-rheumatic suppository as claimed in Claim 1, wherein the inert substance consists of polyethylene glycol.

3. An anti-rheumatic suppository as claimed in Claim 2 wherein the ingredients are mixed in the following proportions by weight: 24 parts salicylic acid, 8 parts calcium carbonate and 160 parts of inert substance.

4. A method of preparing an anti-rheumatic suppository comprising mixing salicylic acid and calcium carbonate, adding to the resultant mixture an inert substance having the necessary consistency of a suppository and thoroughly admixing the same, sterilizing the resultant mixture at about 120 degrees C. for approximately a half hour and permitting the evolved gases to escape.

5. A method of preparing an

anti - rheumatic suppository comprising thoroughly admixing 24 parts by weight of salicylic acid and 8 parts by weight of calcium carbonate, adding to the resultant mixture 160 parts by weight of an inert substance having the consistency of a suppository and thoroughly admixing the same, sterilizing the resulting mixture at about 120 degrees C. for a half hour and permitting the evolved gases to escape.

6. The process according to either of Claims 4 and 5 wherein the inert substance is polyethylene glycol.

BREWER & SON,
Chartered Patent Agents,
5-9, Quality Court, Chancery Lane,
London, W.C.2.

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